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Multiple Vertebral Segmentation Defects: Analysis of 26 New Patients and Review of the Literature

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To further delineate and classify those forms of short trunk dwarfism characterized by multiple vertebral segmentation defects, we analyzed 26 new patients and reviewed 115 described in the literature. Three distinct entities were recognized based on radiographic and clinical findings. Jarcho-Levin syndrome is the lethal autosomal recessive form, characterized by a symmetric crab-like chest. Spondylocostal dysostosis is the benign autosomal dominant condition. Spondylothoracic dysostosis shows considerable clinical and radiographic overlap with spondylocostal dysostosis. Malformations observed in association with multiple vertebral segmentation defects are more common in the sporadic patients. Analysis of the 26 new individuals revealed that the body segment in which these nonvertebral malformations occur corresponds to the site of the vertebral segmentation defects.

KEY WORDS: Jarcho-Levin syndrome, spondylothoracic dysostosis, spondylocostal dysostosis, vertebra segmentation defects

INTRODUCTION

Several types of short trunk dwarfism, characterized by multiple segmentation defects of the vertebral bodies and ribs, have been classified under a variety of terms in the past and there is still considerable semantic and nosological confusion. In 1938, Jarcho and Levin described two sibs with vertebral segmentation defects of the entire vertebral column and fusion of several ribs. Numerous patients with multiple vertebral segmentation defects have since been described under a variety of names including Jarcho-Levin syndrome (MIM#277300), spondylocostal or spondylothoracic dysostosis (dysplasia) and costovertebral dysplasia (MIM#122600). Both autosomal dominant and autosomal recessive forms have been postulated.

Affected individuals have short trunk dwarfism of prenatal onset. The vertebral segmentation defects consist of fusion or absence of vertebrae, hemivertebrae and butterfly vertebrae. The ribs can vary in number and shape. They often show fusion, primarily near the costovertebral ends. In one particular entity, the ribs show a crowded origin from the thoracic vertebral bodies and fan out like the legs of a crab, giving a typical symmetric "crab-like" appearance to the thorax [Pérez-Comas and Garcia-Castro, 1974]. Kyphosis, scoliosis and pectus deformities are due to the multiple vertebral and rib anomalies. Cervical spine involvement is reflected by shortness of the neck and low posterior hairline. In the severe forms, respiratory distress after birth or recurrent respiratory infections lead to early death in infancy. Individuals with the milder forms have problems related to kyphoscoliosis or present in adulthood with low back pain and stiffness of the spine.

MATERIALS AND METHODS

We analyzed the radiographic and clinical findings of 141 patients with multiple vertebral segmentation defects. Twenty-six are newly described patients, who have been collected by the International Skeletal Dysplasia Registry during the past 20 years. The remaining 115 have been reported previously in the literature.

RESULTS

Analysis of Newly Described Patients

The radiographic and clinical features of 26 new patients are illustrated in Table I. The group includes two brothers (cases 19 and 20), one set of monozygotic female twins (cases 5 and 6) and 22 isolated cases. The female/male ratio is 1:1. Patients 1 and 2 had multiple vertebral segmentation defects throughout the spine and a symmetric "crab-like" chest (Fig. 1) without other

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TABLE I. Twenty-Six New Patients With Multiple Vertebral Segmentation Defects

Patient	Sex	Consanguinity	Site of VSD[a]	Crab-like thorax	Number of ribs right/left	Rib fusion	Associated anomalies	Respiratory problems	Survival
1	M	no	CTL	yes	?	yes	none	yes	2 mo[d]
2	M	no	CTLS	yes	10/11	yes	none	yes	3 wks[d]
3	F	no	CTLS	no	6/11	yes	clubfeet, hypoplasia lower limbs, TGA[b] and hypoplasia of the left ventricle, bilobed right lung, cystic kidney, 2 spleens, SUA[c]	yes	2 days[d]
4	M	yes	CT	no	6/9	yes	clubfeet, VSD, omphalocoele, hydronephrosis	yes	1 day[d]
5 (twin A)	F	no	CT	no	10/7	yes	situs inversus	yes	14 mo[d]
6 (twin B)	F	no	CTLS	no	10/12	yes	hypoplasia of left hemipelvis and lower limb, hydronephrosis, imperforate anus	no	alive at 10 y
7	F	no	T	no	10/12	no	none	?	?
8	M	no	TLS	no	11/11	yes	none	no	alive at 13 y
9	F	no	TL	no	12/11	yes	none	no	alive at 5 y
10	F	no	TLS	no	12/12	no	imperforate anus, ambiguous genitalia 47,XXX	no	alive at 7 y
11	M	no	CTLS	no	11/11	no	inguinal hernia, dysplasic sacrum	no	alive at 16 y
12	F	no	CTLS	no	11/12	yes	imperforate anus, clubfeet, absent kidney, unilateral absent pectoralis muscle	?	?
13	M	no	TLS	no	11/12	yes	inguinal hernia	no	alive at 9 y
14	F	no	TLS	no	10/11	yes	none	?	?
15	M	no	TLS	no	12/12	yes	imperforate anus, absent kidney	no	alive at 6 y
16	M	no	CT	no	12/12	yes	none	no	alive at 11 y
17	F	no	T	no	12/12	yes	none	no	alive at 4 y
18	F	no	CTLS	no	7/8	yes	none	?	?
19 (sib 1)	M	no	CTLS	no	8/8	yes	inguinal hernia	yes	alive at 12 y
20 (sib 2)	M	no	CTLS	no	9/8	yes	none	yes	alive at 3 y
21	F	no	CT	no	11/5	yes	cricopharyngeal incoordination	yes	alive at 2 y
22	M	no	TS	no	6/11	yes	absent thumb, absent kidney	yes	alive at 4 mo
23	M	no	CT	no	11/11	yes	hydronephrosis	yes	alive at 8 y
24	F	no	TL	no	9/10	yes	none	?	alive at 6 mo
25	M	no	CTLS	no	12/12	no	hearing loss, clubfeet absent ischia bones	no	alive at 48 y
26	M	no	TL	no	9/10	yes	imperforate anus	?	abortion

[a]VSD, vertebral segmentation defects (C: cervical; T: thoracic; L: lumbar; S: sacral).
[b]TGA, transposition of the great arteries.
[c]SUA, single umbilical artery.
[d]Age at death.

associated anomalies. Both died during infancy because of progressive respiratory failure. The chest configuration of the other 24 varied from almost normal (Fig. 2) to uni- or bilateral severely deformed (Figs. 3 and 4) with the right side most commonly involved. Of those 24, three died during infancy after progressive respiratory failure. Patients 5 and 6 are monozygotic female twins. Their X-rays are illustrated in Figure 5. Patient 5 died at 14 months of age. Her thorax was more affected but she had less vertebral involvement and fewer associated anomalies than her co-twin, patient 6, who is still alive. The structural defects of the caudal region of the body in patient 6 resemble those observed in the caudal regression syndrome, but the

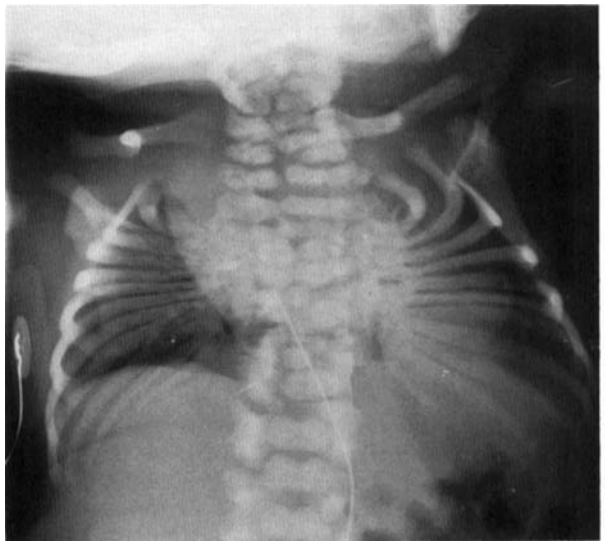

Fig. 1. Anteroposterior radiograph of the thorax in patient 2, illustrating the typical symmetric crab-like chest configuration of Jarcho-Levin syndrome.

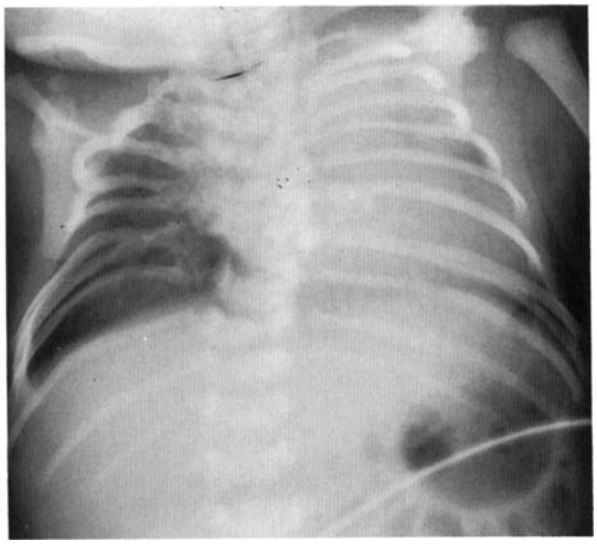

Fig. 3. Anteroposterior radiographic film of the thorax of patient 23. The seventh and eighth rib on the left side are partially fused (cervical rib on the left side). The right hemithorax is more severely affected with fusion of multiple ribs at the costovertebral ends.

vertebral segmentation defects extend over the entire vertebral column and are associated with rib anomalies. Patients 19 and 20 are brothers. They have a similar pattern of vertebral involvement and comparable chest X-rays. Both suffer from recurrent respiratory infections and are still alive at 12 and 13 years of age. They do not have any associated anomalies. The diagnosis of multiple vertebral segmentation defects in patient 26 was made by routine ultrasound examination at 16 weeks gestational age. The parents elected termination of the pregnancy. Autopsy revealed an imperforate anus. Table I also shows that there is no relationship between the lethality of the disorder and the extent of vertebral involvement: patients 4 and 5 only had cervical and thoracic involvement but died early in infancy. In all cases, the prognosis could not be well predicted by an experienced pediatric radiologist based on the chest radiographs only. The chances for survival are probably related more to the pulmonary status and presence of a complex heart malformation than to the thoracic skeletal anomalies.

Table II illustrates the distribution of the vertebral segmentation defects. Multiple thoracic vertebrae are affected in all patients. Exclusive involvement of the

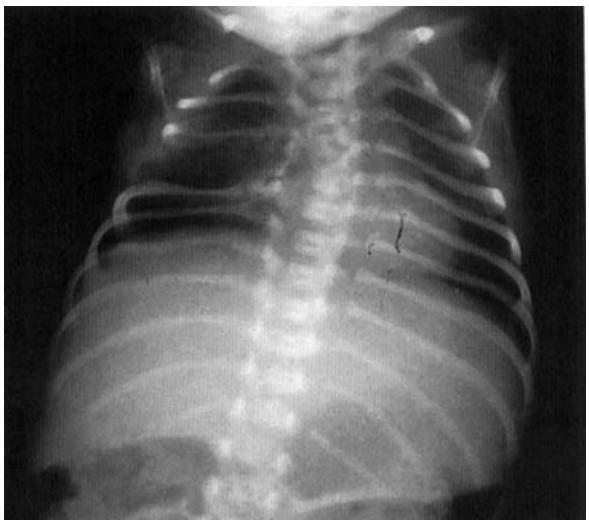

Fig. 2. Anteroposterior radiographic film of the thorax of patient 7, showing only two missing ribs on the right side.

Fig. 4. Anteroposterior view of the chest radiograph of patient 9. Rib fusions are present on both sides. The thoracic and lumbar vertebrae have severe segmentation defects.

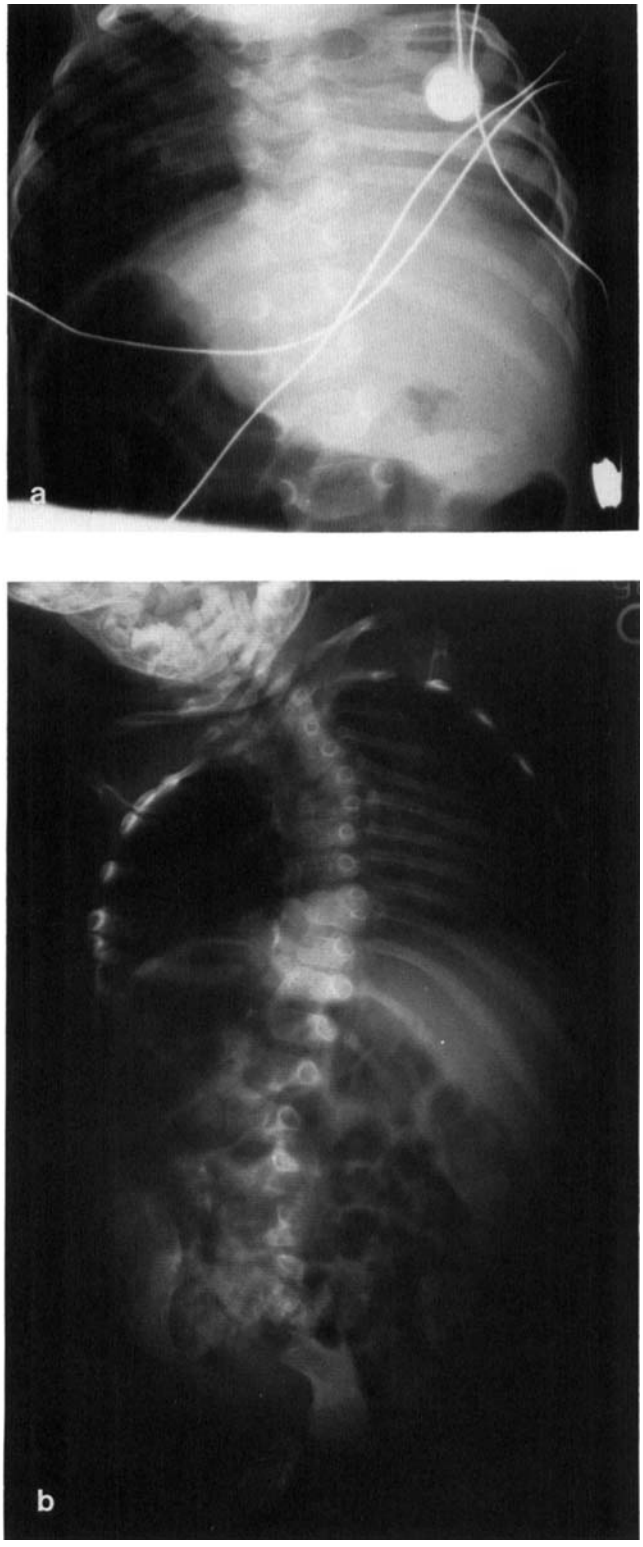

Fig. 5. Disparate involvement in monozygotic female twins. **a:** Anteroposterior view of the chest film of patient 5. Only eight ribs are present on the left side with rib fusions between the first four ribs. This twin died at 14 months. **b:** Anteroposterior view of the radiographic film of the thorax of patient 6. The right hemithorax is more severely affected and deformed than the normal appearing left hemithorax. This twin survived.

TABLE II. Distribution of the Vertebral Segmentation Defects in 26 New Patients With MVSD

	Level of vertebral defects			
% Total cases	Cervical	Thoracic	Lumbar	Sacral
19	*	*		
4	*	*	*	
35	*	*	*	*
8		*		
4		*		*
11		*	*	
19		*	*	*
	58%	100%	69%	58%

thoracic vertebrae is present in only 8%. The entire vertebral column is affected in 35%.

Table III shows the relationship between the vertebral segmentation defects and the associated anomalies. The site of vertebral involvement usually corresponds with the body segment in which the associated malformation occurs. All three patients with a congenital heart defect have thoracic involvement; 3 of 4 patients with clubfeet have lumbar/sacral involvement; all four patients with pelvic abnormalities have lumbar/sacral involvement; 4 of 6 patients with renal abnormalities have lumbar, and 5 of 6 have sacral involvement. All three patients with an inguinal hernia have lumbar involvement. All five patients with an imperforate anus have lumbar involvement and 4 of 5 have sacral involvement.

Analysis of Literature Reports

We reviewed 115 patients with multiple vertebral segmentation defects reported in the literature. Because of insufficient data we did not include those reported by Herold et al. [1988], Marks et al. [1989], Marti et al. [1988] or Waaler and Aarskog [1980].

Only 20 patients had a typical symmetric "crab-like" chest (Table IV). They all died before 2 years of age because of respiratory insufficiency, except for one individual who also had single transverse palmar creases and a posterior membranous cleft palate (case 6, Pérez-Comas and Garcia-Castro [1974]). The radiographic film of the thorax of the latter patient was not shown in the paper. Fourteen patients were of Puerto Rican ancestry. Recurrence in sibs with unaffected parents and/or consanguinity suggests autosomal recessive inheritance. A posterior membranous cleft palate, spina bifida, herniae and hydronephrosis (due to slight narrowing of the right ureter) were the only reported associated malformations. Although it was often difficult to estimate the extent of vertebral involvement from the figures in the reports, segmentation defects throughout the entire vertebral column seemed to be a feature common to all patients.

In the group of patients without a symmetric crab-like chest, two families clearly showed an autosomal recessive mode of inheritance [Cantu et al., 1971; Turnpenny et al., 1991] (Table V). In the family reported by Cantu et al. [1971], five individuals in one generation were affected. They were offspring from two different

TABLE III. Associated Anomalies and Site of Vertebral Involvement in 26 New Patients With MVSD

	Site of vertebral involvement			
Associated anomalies (frequency)	Cervical	Thoracic	Lumbar	Sacral
Heart (11%; n = 3)				
[a]VSD	*	*		
dextrocardia	*	*		
[b]TGA and hypoplastic left ventricle	*	*	*	*
Limbs (19%; n = 5)				
absence of thumb		*		*
clubfeet	*	*		
	*	*	*	*
	*	*	*	*
	*	*	*	*
Pelvis (15%; n = 4)				
hypoplasia of pelvis	*	*	*	*
or limb	*	*	*	*
	*	*	*	*
absence of ischial bone	*	*	*	*
Kidney (23%; n = 6)				
absence of kidney		*		*
		*	*	*
	*	*	*	*
hydronephrosis	*	*		
	*	*	*	*
	*	*	*	*
Herniae (15%; n = 4)				
inguinal hernia		*	*	*
	*	*	*	*
	*	*	*	*
omphalocele	*	*		
Ambiguous genitalia (4%; n = 1)		*	*	*
Imperforate anus (19%; n = 5)	*	*	*	
	*	*	*	*
		*	*	*
		*	*	*
		*	*	

Each line of asterisks represents one patient with the associated anomalies.
[a]VSD, ventricular septal defect. [b]TGA, Transposition of great arteries.

pairs of consanguineous parents related to a common ancestor. Three died during infancy due to respiratory infections and two are still alive at ages 9 months and 6 years. In none were associated anomalies reported. Autopsy was not performed in the proband. The family reported by Turnpenny et al. [1991] consists of seven affected individuals in two generations of a large inbred Arab kindred. The propositus (case 4) died at 6 months of age because of cardiorespiratory failure. At necropsy he was found to have a large patent ductus arteriosus, right ventricular hypertrophy (secondary to pulmonary hypertension) and a membranous left diaphragm. The other relatives are still alive. They did not have a history of recurrent respiratory infections and did not show major associated anomalies. The plagiocephaly-torticollis sequence described in 5 of the 7 patients was probably secondary to cervical vertebral anomalies.

Eight families with vertical transmission, suggestive of autosomal dominant inheritance, have been described [van der Sar, 1952; Rütt and Degenhordt, 1959; Peralta et al., 1967; Rimoin et al., 1968; Kubryk and Borde, 1981; Temple et al., 1988; Floor et al., 1989; Lorenz and Rupprecht, 1990]. All were alive at the time of reporting. Associated major anomalies were absent. The patients usually presented with scoliosis, short trunk dwarfism, low back pain or decreased mobility of the spine. Respiratory difficulties during infancy were usually absent, although the propositus reported by Lorenz and Rupprecht [1990] presented with respiratory distress after birth and required tube-feeding for 10 weeks because of respiratory problems. The affected individual reported by Peralta et al. [1967] also had respiratory problems during feeding in early infancy.

Table VI illustrates 36 patients in whom an autosomal recessive mode of inheritance was suspected because of recurrence in sibs and/or consanguinity of the parents. Eight affected individuals died in infancy. Three had associated anomalies. Major associated anomalies were absent in those who survived.

Twenty-seven sporadic patients are documented in Table VII. Ten died before 15 months of age. All but one had associated anomalies. Twelve were alive at time of reporting, of which seven had major associated malformations. Two reports deserve additional comments. The first is the report of Casamassima et al. [1981]. This affected individual had multiple vertebral seg-

TABLE IV. Patients With MVSD and a Symmetric "Crab-like" Chest

Author	Patients	Ethnicity	Consanguinity	Associated anomalies	Survival
Lavy et al. [1966]	sib 1	PR[a]	yes	none	† 6 months
	sib 2	PR	yes	none	† 6 months
	sib 3	PR	yes	none	† 17 days
	sib 4	PR	yes	none	† 1 day
Moseley and Bonforte [1969]	case 2	PR	no	absent anal reflex	† 1 month
Pérez-Comas and Garcia-Castro [1974]	case 1	PR	no	inguinal hernia	† 6 months
	case 2	PR	no	umbilical hernia	† 13 months
	case 3	PR	no	none	† 6 months
	sib 1	PR	no	none	?
	sib 2	PR	no	none	† 25 days
	case 6	PR	no	simian creases, cleft palate	alive
Pochaczevsky et al. [1971]	case 2	PR	no	hydronephrosis	† 4 months
Solomon et al. [1978]	sib 1	PR	no	none	† 17 days
	sib 2	PR	no	spina bifida	† 31 days
Bonaime et al. [1978]	sib 1	Caucasian	?	none	† 19 months
	sib 2	Caucasian	?	inguinal hernia	† 15 days
Ho [1992]	case 1	Chinese	no	inguinal hernia, abdominal wall hernia	† 66 days
Rome et al. [1991]	4th degree relative	Sicilian	no	inguinal hernia, simian creases	† 3 months
	sib 1	Sicilian	no	inguinal hernia	† 50 days
	sib 2	Sicilian	no	inguinal hernia	† 40 days

[a]PR, Puerto Rican ancestry.
†died.

mentation defects in addition to a single umbilical artery, left inguinal hernia and anal atresia. The family history was remarkable for a stillborn brother with short neck and trunk, absent external genitalia, anal atresia and urethral atresia. Although no radiographs were available on the stillborn fetus, both sibs were diagnosed with a distinct entity of spondylocostal dysostosis, anal atresia, and urogenital anomalies (MIM#271520). Since no radiographs were available on the fetus to document multiple vertebral segmentation defects, we consider the affected sib to be an isolated case and the fetus to have features of the urorectal septal malformation sequence. The shortness of the chest could be secondary to massive abdominal wall distension, which was caused by bilateral hydroureteronephrosis as a consequence of urethral atresia (urethral obstruction sequence).

The second report of interest is the female infant described by Eller and Morton [1970]. She had multiple vertebral segmentation defects and died of respiratory insufficiency at the age of 40 days. Roentgenograms revealed craniolacunae in addition to the multiple vertebral segmentation defects. Cystogram demonstrated a persistent urachus and a rectovesical fistula. Autopsy revealed a horseshoe kidney, single midline adrenal gland, and Arnold-Chiari malformation with hydro-

TABLE V. Two Families With MVSD and *Clearly* Autosomal Recessive Inheritance

Author	Patients[a]	Ethnicity	Consanguinity	Associated anomalies	Survival
Turnpenny et al. [1991]	1 (V-3)	Arab	yes	inguinal hernia	alive
	2 (V-4)	Arab	yes	none	alive
	3 (V-5)	Arab	yes	none	alive
	4 (VI-1)	Arab	yes	inguinal hernia, large PDA,[b] membranous left diaphragm	6 months[c]
	5 (VI-2)	Arab	yes	inguinal hernia	alive
	6 (VI-3)	Arab	yes	inguinal hernia	alive
	7 (V-8)	Arab	yes	none	alive
Cantu et al. [1971]	1 (V-4)	?	yes	none	4 months[c]
	2 (V-1)	?	yes	none	alive
	3 (V-8)	?	yes	none	alive
	4 (V-5)	?	yes	?	early[c]
	5 (V-6)	?	yes	?	early[c]

[a]Patients, pedigree symbols in original report are mentioned between parentheses.
[b]3 PDA, patent ductus arteriosus.
[c]Age at death.

TABLE VI. Thirty-Six Patients With MVSD and *Suggestive* Autosomal Recessive Inheritance

Author	Patient	Consanguinity	Associated anomalies	Survival
Beighton and Horan [1981]	sib 1	no	none	alive ?
	sib 2	no	none	alive ?
Caffey [1967]	sib 1	?	none	alive
	sib 2	?	none	alive
Castroviejo et al. [1973]	sib 1	no	none	alive
	sib 2	no	none	alive
	sib 3	no	none	alive
David and Glass [1983]	sib 1	no	inguinal hernia	alive
	sib 2	no	none	alive
Fogarty et al. [1985]	twin a	no	none	?
	twin b	no	none	?
Franceschini et al. [1974]	sib 1	yes	postaxial hexadactyly, Fallot's tetralogy	6 months[a]
	sib 2	yes	macroglossia, clubfeet	alive
Jarcho and Levin [1938]	sib 1	?	none	6 months[a]
	sib 2	?	none	19 days[a]
Lakshminarayana et al. [1992]	sib 1	yes	none	3 months[a]
	sib 2	yes	none	termination
Norum and McKusick [1969]	sib 1	?	none	alive
	sib 2	?	none	alive
	sib 3	?	none	alive
	case 1	yes	none	alive
Poor et al. [1983]	sib 1	no	uterus didelphys, cerebral polygyria, single umbilical artery	1 day[a]
	sib 2	no	none	3 days[a]
	sib 3	no	single umbilical artery	termination
Roberts [1988] Tolmie et al. [1987]	sib 1	no	hydronephrosis, absent kidney, absent hemidiaphragma	after birth[a]
	sib 2	no	imperforate anus	termination
	sib 1	no	none	alive
	sib 2	no	none	alive
	case 1	yes	none	alive
Satar et al. [1992]	MZ twin a	yes	?	?
	MZ twin b	yes	?	?
Silengo et al. [1978]	sib 1	no	none	alive
	sib 2	no	none	alive
Trindade and de Nobrega [1977]	sib 1	no	none	alive
	sib 2	no	none	4 months[a]
Young and Moore [1984]	case 1	yes	none	?

[a] Age at death

cephalus and fusion of the frontal lobes of the brain. She represents the only patient discussed in the literature in which substance abuse during pregnancy was documented: the 19-year-old mother admitted to the use of LSD on a single occasion at about the time of conception. She also smoked cigarettes and used an estrogen preparation to induce menstruation early in the first trimester.

DISCUSSION

Considerable confusion has existed concerning the nomenclature of syndromes characterized by multiple segmentation defects of the vertebrae. After Jarcho and Levin described two sibs with "hereditary malformations of the vertebral bodies" in 1938, several similar patients have since been described with a variety of diagnoses. Lavy et al. [1966] reported four sibs, offspring of third cousins, and called the disorder "a syndrome of bizarre vertebral anomalies." Moseley and Bonforte [1969] introduced the term "spondylothoracic dysplasia." Following the description of a black mother and daughter with short trunk dwarfism by van der Sar [1952], Rimoin et al. [1968] described a second family with evidence of a dominantly inherited form and pro-

TABLE VII. Twenty-Seven Sporadic Patients With MVSD

Author	Patient (case no.)	Associated anomalies	Survival
Bonaime et al. [1978]	3	inguinal hernia, hydronephrosis	alive
	4	ectopic kidney	alive
	5	inguinal hernia, absent kidney	alive
	6	inguinal hernia	alive
	7	none	alive
Casamassima et al. [1981]	1	inguinal hernia, imperforate anus, SUA[a]	alive
Delgoffe et al. [1982]	1	complex cardiac malformation, megaloureter	early[b]
	2	ventricular septal defect, SUA[a]	alive
	3	anomalous pulmonary venous return, SUA[a]	early[b]
	4	Fallot's tetralogy, megaloureter	?
Devos et al. [1978]	1	bilateral hydronephrosis due to duplication of intrarenal collecting system and abnormal bladder implantation of ureters	alive
Eller and Morton [1970]	1	meningomyelocoele, horseshoe kidneys, persistent urachus, rectovesical fistula, single midline adrenal gland, central nervous system anomalies	40 days[b]
Giacoia and Say [1991]	1	atrium septum defect, cleft palate, imperforate anus, diastematomyelia, meningomyelocoele, aqueductal stenosis	alive?
Heilbronner and Renshaw [1984]	1	none	?
Karnes et al. [1991]	1	preauricular skin tags, clubfeet, horseshoe kidneys, 2 spleens, unicornulate uterus	5 days[b]
	2	absent kidney, SUA[a] preauricular skin tags	3 months[b]
	3	none	alive
	4	meningomyelocoele, supernumerary nipple	4 months[b]
Lin and Harster [1993]	1	absent kidney, imperforate anus, meningomyelocoele, cerebral polygyria, SUA,[a] clubfeet, cystic kidneys	stillborn
Moseley and Bonforte [1969]	1	none	15 months[b]
Murr et al. [1992]	1	imperforate anus, SUA, clubfeet, cystic kidneys, preauricular skin tags, preaxial polydactyly	1 day[b]
Ohzeki et al. [1990]	1	mesocardia	?
Pochaczevsky et al. [1971]	1	bilobed bladder	6 months[b]
	3	none	?
Reyes et al. [1989]	1	diastematomyelia, clubfeet	45 days[b]
Roberts [1988]	6	none	alive
	7	cyanotic heart disease (?)	alive

[a] SUA, single umbilical artery.
[b] Age at death

posed the distinguishing term "spondylocostal dysplasia." Cantu et al. [1971] called the condition "costovertebral dysplasia." Because of the apparent multisystem involvement, Pérez-Comas and Garcia-Castro [1974] used the descriptive term of "occipito-facial-cervicothoracic-abdomino-digital dysplasia" or "Jarcho-Levin syndrome of vertebral anomalies." They emphasized the lethality of the condition, the Puerto Rican ethnic background and the "crab-like" appearance of the thorax. Because the vertebral defects represent a malformation rather than a generalized skeletal disorder, all the cases were classified in the International Nomenclature of Constitutional Disorders of Bone as dysostoses rather than dysplasias [Maroteaux, 1970; McKusick and Scott, 1971]. Subsequently, Solomon et al. [1978] introduced the term "spondylothoracic dysostosis" and Young et al. [1984] the description "spondylocostal dysostosis."

Several classifications of MVSD (multiple vertebral segmentation defects) have been proposed in previous reports. These have been based on severity, apparent mode of inheritance and radiologic image of the thorax. Rimoin et al. [1968] concluded that there were at least two distinct genetic disorders, a clinically benign form, inherited as an autosomal dominant trait, and a severe autosomal recessive form, associated with early death

from respiratory complications. Subsequently, reports of patients with a normal life span and apparent autosomal recessive inheritance appeared [Cantu et al., 1971; Turnpenny et al., 1991]. Solomon et al. [1978] subdivided all cases into just two groups. Patients with a crab-like thorax, absence of intrinsic rib anomalies, and early death in infancy were classified in the group of spondylothoracic dysostosis. Autosomal recessive inheritance was proposed because of recurrence in sibs and/or consanguinity of the parents. The second group was called spondylocostal dysostosis. Affected individuals with this condition did not have a crab-like thorax but showed costal anomalies consisting of broadening, bifurcation and fusion of several ribs. Both autosomal dominant and recessive patterns of inheritance were suggested and most of the patients were alive at the time of reporting. However, Karnes et al. [1991] noted the presence of rib anomalies in some individuals with spondylothoracic dysostosis. Ayme and Preus [1986] performed a cluster analysis on 30 patients reported in the literature and found three clusters. One cluster consisted of patients with Robinow syndrome, a different disorder. Exact criteria for classification into the two other clusters were not included in their discussion.

Our analysis of 26 newly described patients and review of the literature allows the definition of at least three distinct types of short trunk dwarfism with multiple vertebral segmentation defects and rib anomalies.

The first entity is characterized radiographically by a symmetric crab-like thorax, as described by Pérez-Comas and Garcia-Castro [1974]. The ribs show a crowded origin from the deformed thoracic vertebral bodies and fan out like the legs of a crab. Vertebral segmentation defects usually involve the entire vertebral column. Death from respiratory infections before the age of 2 years is the rule. Other *major* congenital malformations are usually absent. Recurrence in sibs and/or consanguinity of the parents suggest autosomal recessive inheritance. Puerto Rican ethnic background is common. This condition has been called Jarcho-Levin syndrome in the literature, although the sibs reported by Jarcho and Levin in 1938 did not really have a crab-like chest.

The second entity, frequently called "spondylo*thoracic* dysostosis," has an autosomal recessive mode of inheritance. Intrafamilial variability is striking [Cantu et al., 1971; Franceschini et al., 1974; Trindade and de Nobrega, 1977; Turnpenny et al., 1991]. Affected individuals either die in infancy of respiratory failure or survive into adulthood with minimal symptoms. Associated anomalies are not common and are only observed in the lethal cases.

The third distinct entity has an autosomal dominant mode of inheritance and has previously been called spondylo*costal* dysostosis. Patients with spondylocostal dysostosis seem to have a normal lifespan and lack of associated anomalies. There usually is no history of respiratory problems. Affected individuals present after infancy with problems related to kyphoscoliosis, low back pain, or decreased mobility of the spine. Although the segmentation anomalies tend to be milder in patients with spondylocostal dysostosis, multiple vertebral segmentation defects throughout the entire spine, in addition to fusion and/or absence of several ribs, can be observed in both spondylocostal and spondylothoracic dysostosis.

Sporadic patients are difficult to classify as to etiology (genetic vs. nongenetic). They probably represent a heterogeneous group. The radiographic features do not differ substantially from those observed in spondylocostal and spondylothoracic dysostosis. Associated anomalies are more common than in the familial types and can involve both mesodermally and ectodermally derived structures. In this group, individuals with a normal lifespan and absence of associated anomalies may have either spondylocostal or spondylothoracic dysostosis. Those with associated anomalies are affected either by spondylothoracic dysostosis or a different nongenetic condition.

Analysis of 26 new patients illustrates that the body segment in which an associated anomaly occurs usually corresponds to the site of vertebral segmentation defect. The same conclusion could not be made by analyzing the reports in the literature because of insufficient data.

Conditions with multiple vertebral segmentation defects are a heterogeneous group of disorders among which at least three distinct classes can be recognized. Considerable clinical and radiographic overlap between the spondylocostal and spondylothoracic dysostoses makes accurate genetic counseling difficult in sporadic patients without associated anomalies. Major anomalies in association with multiple vertebral segmentation defects were found primarily in the sporadic cases and only occasionally in the familial cases. In the absence of a typical symmetric crab-like chest configuration, the prognosis may be difficult to establish in the newborn period based on the chest X-ray film only.

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